REMARKS

Claims 1-3, 5-8, 11 and 14-15 are under examination. By the foregoing amendments, claims 1, 3 and 8 have been amended and claim 2 has been canceled. Claims 4, 7 (partially), 9-10, 12-13 and 16 are withdrawn from further consideration as directed to non-elected species. It is Applicant's understanding that claim 11 is not partially or fully withdrawn from consideration.

Applicant acknowledges with thanks the Examiner's partial withdrawal of the election of species requirement with respect to G protein coupled receptors (claim 11).

The Rejection under 35 USC 112, First Paragraph

Claims 1-3, 5-8, 11 and 14-15 stand rejected under Section 112, first paragraph, because they are allegedly not fully described in the description. The Examiner argues that the specification provides insufficient detail of the claimed invention because the Example is prophetic and no bivalent molecules are actually obtained. The definition of "bivalent binding molecule" in the specification does not provide any structure or formula for a single bivalent binding molecule. The Examiner cites *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997), which states that the written description for a chemical genus "requires a precise definition, such as by structure, formula [or] chemical name of he claimed subject matter sufficient to distinguish it from other materials." Applicant respectfully traverses this rejection.

The Applicant respectfully submits that the subject specification provides a detailed description of the claimed subject matter. On pages 7-8, the specification provides that the bivalent binding molecule can be an aptamer coupled to a non-aptamer binding domain (directly or via a linker). The non-aptamer binding domain can be an antibody or antibody fragment, or may be all or a portion of a naturally occurring ligand of the 7 TM G protein coupled receptor. An aptamer is described on page 12 as a nucleic acid ligand having specific binding affinity for an epitope on an extracellular membrane portion of a 7 TM G protein coupled receptor (page 12, third paragraph). A nucleic acid means DNA, RNA, single-stranded or double-stranded and any chemical modifications thereof, wherein the possible modifications are described in detail at page 12, paragraph 4

to page 13, paragraph 1. Examples of non-aptamers are set forth at page 24, third paragraph, and include:

> antibodies, proteins (including peptides and polypeptides), or their derivatives, including, but limited to, hormones, antigens, synthetic or naturally occurring drugs, and the like; opiates; dopamine; serotonin, catecholamines; thrombin; acetylcholine; prostaglandins; small molecules such as fragrances; pheromones; adenosine; simple sugars such as sucrose, glucose, lactose and galactose, and any other moieties that recognize and have affinity toward an epitope of a 7 TM G protein-coupled receptor.

Applicant also respectfully points out that the subject application claims priority to and incorporates by reference, Biesecker et al., U.S. 5,683,867. This patent describes and exemplifies bivalent binding molecules using the blended SELEX method, which is also set forth in detail at pages 23-24 of the subject specification. The '867 patent exemplified in its Example 2 how to obtain a bivalent binding molecule by using the blended SELEX method to obtain bivalent molecules to gpIIb,IIIa. In Example 3 of the '867 patent, a bivalent binding molecule to elastase is obtained, and the aptamer sequence is set forth in SEQ. ID. NO. 3. While neither elastase nor gpIIb,IIIa is a 7 TM G protein coupled receptor, the method exemplified in the '867 patent, when read with the subject specification, provides ample written description of how a bivalent binding molecule to a 7 TM G protein coupled receptor can be obtained. Moreover, the '867 patent provides at col. 7, lines 3-5, that blended SELEX can be used on a number of target species, including those that are not nucleic acid binding proteins (which would include 7 TM G protein coupled receptors). It is therefore respectfully submitted that the subject specification by itself and/or in association with description provided in the '867 patent, adequately describes the genus of chemical compounds set forth in claim 1.

Applicant further respectfully points out that the case law relied upon by the Examiner, is relevant only to the specific facts set forth in that case. Specifically, the holding of the *University of California, supra*, is submitted to be relevant only to those situations where the claimed gene species or genus at issue encodes a functional protein or polypeptide. In a situation where a gene or a genus of genes is being claimed as a composition, it can be seen how specific sequences may be necessary to demonstrate

possession of the invention. However, in the subject case, it is not necessary to set forth in the specification a sequence of the aptamer portion of the bivalent binding molecule because it has already been established in the '867 patent that such bivalent molecules can be obtained using the methods described in the subject application and the '867 patent.

It is inappropriate to apply law established with respect to genes to nucleic acid ligands (now commonly referred to in the art as "aptamers"). Aptamers are chemical entities that form three-dimensional structures capable of binding virtually any target. As such, aptamers are analogous to monoclonal antibodies. The fact that genes and aptamers are both comprised of nucleic acids does not make them similar in function.

It is not necessary to provide a specific sequence to claim a class of monoclonal antibodies. In the same way, aptamers are a recognized class of chemical compounds that exhibit the property of binding to a specified target. As with antibodies, even though specific sequences are not set forth in the subject specification, it is clear that the use of the described methods will produce aptamers to 7 TM G protein coupled receptor. Applicant therefore respectfully requests withdrawal of the Section 112, first paragraph, rejection.

The Rejection Under 35 USC § 102

Claims 1, 6 and 11 are rejected under Section 102(a) as anticipated by Lerner et al., WO 98/03632. The Examiner notes that the rejection is based on the broadly claimed bivalent molecule, where at least one of the binding molecules is not an aptamer. The Examiner also states that Applicant is not entitled to the priority date of the Biesecker et al. patent, U.S. 5,683,867, because it allegedly does not disclose a bivalent binding molecule to a 7 TM G protein coupled receptor.

Applicant does not acquiesce in the Examiner's characterization of Biesecker et al. However, in keeping with the election of species requirement, has amended claim 1 to recite the species of claim 2, i.e., that at least one binding domain is an aptamer. Applicant respectfully points out that the "ligand domains" of Lerner et al., which are defined in the paragraph spanning pages 10-11 of WO 98/03632, do not mention or

suggest that the ligand domains may be nucleic acid ligands. For the foregoing reasons, it is respectfully requested that the Section 102 rejection be withdrawn.

The Rejection Under 35 § 103

Claims 1-3, 5-8, 11 and 14-15 stand rejected over Biesecker et al., U.S. 5,683,867, in view of Lerner et al., WO 98/03632 and Toole et al., WO 92/14843.

The Examiner identifies several ways of addressing the Biesecker et al. reference, which is prior art only under Sections 102(e)/103(a). In keeping with one of the Examiner's suggestions, Applicant submits a 37 CFR § 1.132 Declaration which provides that to the extent the subject application was disclosed in the prior application, it was not the invention of the inventors named in that prior application, but is instead the invention of the inventors of the subject application, and is therefore not an invention "by another" as provided in Section 102(e). Applicant submits that the Section 132 Declaration removes Biesecker et al. as prior art.

Lerner al. does describe 7 TM G protein coupled receptors and bivalent agonists thereto, wherein the bivalent agonists comprise two ligand domains and a molecular backbone. However, the ligand domains are never described in terms of being aptamers or nucleic acid ligands (see page 11, first paragraph).

Toole et al. does describe aptamers, and lists hundreds of possible targets in Table 1 at the end of the specification. The Examiner argues that Table 1 includes gpIIb,IIIa and bradykinin (which is also exemplified), which are supposedly 7 TM G protein coupled receptors. Actually, it is the bradykinin receptor and the gpIIb,IIIa receptor that are 7 TM G protein coupled receptors. These receptors do not appear to be disclosed in Toole et al. Even if we were to assume (without conceding) that Table 1 of Toole et al. might contain one or a few 7 TM G protein coupled receptors, Table 1 at most represents a list of possible experiments that may be obvious to try. It is well established that "obvious to try" is not the appropriate standard for establishing obviousness under Section 103 (*In re O'Farrell*, 7 USPQ2d 1673 (Fed. Cir. 1988)).

Thus, Applicant respectfully submits that there is insufficient motivation in the prior art to combine the elements of Toole et al. and Lerner. et al. At most, any such

combination would have hinted at possible experiments that might have been obvious to try. For these reasons, the Applicant respectfully submits that *prima* facie obviousness has not been established and therefore request withdrawal of the subject rejection.

The Rejection Under the Doctrine of Obviousness-Type Double Patenting

Claims 1-3, 5-8, 11 and 14-15 stand rejected under the doctrine of obviousness type double patenting over claims 6, 7, 10-11 and 14 of Biesecker et al. U.S. 5,683,867 in view of Lerner et al., WO 98/03632 and Toole et al., WO 92/14843.

Applicant agrees to file a Terminal Disclaimer over Biesecker et al. when allowable claims are indicated in the subject application.

Closing Remarks

It is believed that the subject application is now in condition for allowance and notification of same is respectfully requested. If the Examiner believes that a phone conference would expedite prosecution, she is invited to phone the undersigned at 303-268-0066.

Submitted herewith is a Petition for Extension of Time for 1 month and a check for $120. It is believed that no other fees are due with this submission. If this is in error, please charge any necessary fees to Deposit Account No. 19-5117.

Respectfully submitted,

Date July 8, 2005

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Attachment: Declaration under 1.132 of Larry Gold

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